Respiratory Medicine (2011) 105, 595–601

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/rmed

Hospital admissions related to acute exacerbations of chronic obstructive pulmonary disease in France, 1998–2007

Claire Fuhrman [a,*], Nicolas Roche [b], Alain Vergnenègre [c], Mahmoud Zureik [d], Christos Chouaid [e], Marie-Christine Delmas [a]

[a] Institut de veille sanitaire, 12 rue du Val d'Osne, 94415 Saint-Maurice Cedex, France
[b] Pneumologie et Réanimation, Hôtel-Dieu, AP-HP, Université Paris Descartes, Paris, France
[c] Hôpital le Cluzeau, Limoges, France
[d] Inserm U700, Université de médecine Bichat, Paris, France
[e] Hôpital Saint-Antoine, AP-HP, Paris, France

Received 3 August 2010; accepted 14 November 2010
Available online 3 December 2010

KEYWORDS
COPD;
Exacerbation;
Hospitalization;
Epidemiology;
Surveillance

Summary
Background: Acute exacerbations of chronic obstructive pulmonary disease (AE-COPD) necessitating hospital admission have a major impact on patient outcome and management costs. We examined temporal trends in AE-COPD-related hospital admissions in France between 1998 and 2007.
Methods: Data were obtained from the French national hospital discharge database for patients aged at least 25 years. AE-COPD was identified with both a "narrow" and a "broad" definition, according to the position (primary or associated) of diagnoses, in order to ensure robustness.
Results: In 2007, among adults aged 25 years or more, the crude AE-COPD-related admission rates were 23/10000 in men and 10/10000 in women using the narrow definition. Using the broad definition, these rates were respectively 38 and 16/10000. With the narrow definition, the annual number of AE-COPD-related admissions increased by 38% between 1998 and 2007, while in-hospital lethality decreased from 7.6% to 6.0%. The proportion of male patients decreased from 72% to 68%. Similar trends were found using the broad definition. The age-standardized AE-COPD-related admission rate increased by 4.4% per year in women and by 1.6% per year in men with the narrow definition, and by respectively 3.8% and 1.2% with the broad

* Corresponding author. Tel.: +33 (0)1 55 12 53 30; fax: +33 (0)1 41 79 68 11.
E-mail address: c.fuhrman@invs.sante.fr (C. Fuhrman).

doi:10.1016/j.rmed.2010.11.014

definition. A strong seasonal pattern of admissions for AE-COPD was found, matching that of general practitioners visits for influenza-like illness.
Conclusion: Hospitalization rates for AE-COPD have increased in France in recent years, especially among women. By contrast, AE-COPD-related in-hospital lethality has decreased.

Introduction

The prevalence of chronic obstructive pulmonary disease (COPD) ranges from 5% to 15% in industrialized countries,[1,2] and the burden of COPD in terms of disability and mortality is expected to rise.[3] Reported management costs are highly variable, but COPD is clearly an important source of health care expenditure. In 1993, COPD was the second source of total costs and the first source of direct medical costs among all pulmonary disorders in the United States,[4] while it accounted for 3.5% of total medical expenditure in France in 2001.[5]

Attempts have been made to increase awareness of COPD in the general population and also among doctors and health authorities, and to improve COPD prevention, diagnosis and management.[6] The final goal of these initiatives is to reduce the morbidity, mortality and costs of COPD. In France, the international GOLD initiative (Global Initiative for Chronic Obstructive Lung Disease) has been relayed by the health authorities, scientific societies, professional bodies and patient associations. In 2005 the French Ministry of Health launched a 5-year plan against COPD, with six main priorities: to improve epidemiological knowledge of COPD; to improve public information; to educate healthcare providers; to facilitate access to care and to improve quality of care; to develop patient education and rehabilitation programs and structures; and to support research.[7]

International and French initiatives have underlined the need to develop indicators for assessing the COPD burden and for monitoring trends. AE-COPD-related hospital admissions could serve as such an indicator, and may reflect the impact of global and targeted preventive and therapeutic measures.

Acute exacerbations of COPD (AE-COPD) are major events in the disease course, especially when they necessitate hospitalization. Indeed, AE-COPD is associated with a decline in lung function, impaired health-related quality of life, and increased mortality.[8,9] Hospitalizations for AE-COPD account for a large proportion of COPD-related healthcare expenditure. The French SCOPE study showed that, among patients with diagnosed and treated COPD in the early 2000s, 41% of total medical resource consumption was directly related to COPD care, 34% to comorbid illnesses, and 25% to exacerbations.[10] The frequency and severity of AE-COPD could be reduced by early diagnosis, education in self-management, and home-based care.[11,12]

National hospital discharge databases are a useful ongoing source of data on the burden of AE-COPD. However, AE-COPD can be designated by various combinations of codes of the International Classification of Diseases (ICD). A French expert committee proposed two definitions for identifying AE-COPD.[13] The aim of this study was to document trends in hospital admissions for AE-COPD between 1998 and 2007, based on the French national hospital discharge database.

Methods

Data sources

Data were extracted from the French hospital discharge database (PMSI) for all patients aged 25 years or more admitted from 1998 to the end of 2007 to hospitals located in metropolitan France. The database covers all public and private French hospitals. It includes both administrative data (age, sex, zip code of the area of residence, admission and discharge dates) and medical information, including primary and associated diagnoses and vital status at discharge. To ensure confidentiality, admission and discharge dates are replaced with the length of stay (LOS) and the month of discharge. Until 2009, the primary diagnosis was defined as the diagnosis for which most medical resources were used. Diagnoses are coded according to the ICD 10th revision (ICD-10). As linkage between records for a given patient was not available for the entire study period, the present analysis focused on records rather than individuals. Records with an LOS shorter than two days were excluded unless the discharge status was "deceased", in order to eliminate day hospitalization and short stays for scheduled examinations.

Incidence rates of general practitioner (GP) visits for influenza-like illness were provided by the French Sentinelles network (www.sentiweb.fr).[14] Influenza-like illness was defined as sudden onset of fever ($\geq$39 °C), with myalgia and respiratory symptoms.

Definitions of AE-COPD

The two ICD10-based definitions of AE-COPD proposed by the French expert committee are described in Table 1.[13] These two definitions differed in the place (primaryor associated) of diagnoses. The "narrow" definition included records with a primary diagnosis of AE-COPD (specific codes J44.0 or J44.1) and those combining (i) a diagnosis of COPD or emphysema and (ii) a lower respiratory tract infection (LRTI) or acute respiratory failure (ARF), with one of these codes (COPD, emphysema, LRTI or ARF) being cited as the primary diagnosis. The "broad" definition included all records with the previous codes or combination of codes, without taking into account the type of diagnosis (i.e. primary or associated), and records with a primary diagnosis of COPD or emphysema (J44 or J43).

Statistical analysis

Population data provided by the French National Institute for Statistics and Economic Studies (INSEE) were used to calculate the crude and 5-year age-specific admission rates for each calendar year. Age-standardized rates (direct method) were calculated by applying the age-specific hospitalization rates to the 2006 French population.

Table 1 Algorithm used to identify hospital admissions for COPD exacerbations.

Narrow definition	- primary diagnosis of COPD with acute lower respiratory infection (J44.0) or - primary diagnosis of COPD with acute exacerbation, unspecified (J44.1) or - primary diagnosis of acute respiratory failure (ARF, J96.0) with an associated diagnosis of emphysema (J43*) or COPD (J44*) or - primary diagnosis of acute lower respiratory infections (LRI, J10-J18, J20-J22) with an associated diagnosis of emphysema (J43*) or COPD (J44*) or - primary diagnosis of emphysema (J43*) or COPD (J44*) with an associated diagnosis of ARF or LRI
Broad definition	- primary diagnosis of emphysema (J43*) or COPD (J44*) or - associated diagnosis of COPD with acute lower respiratory infection (J44.0) or with acute exacerbation (J44.1) or - ARF (J96.0) with emphysema (J43*) or with COPD (J44*), whatever the type of diagnosis (i.e. primary or associated) or - LRI (J10-J18, J20-J22) with emphysema (J43*) or with COPD (J44*), whatever the type of diagnosis (i.e. primary or associated)

Trends over time were analyzed by using age-standardized annual rates calculated for 12-month periods from 1 July to 30 June of the following year, to take into account the seasonal pattern of AE-COPD. The annual percentage changes (APC) in hospitalization rates and their confidence intervals (CI) were estimated with Poisson regression models. The models included a linear time trend and a qualitative age effect. An interaction term between sex and year was also introduced in the model to test for between-gender differences in time trends. The threshold of significance was set at 1%.

Results

Number of admissions and mortality

In 2006—2007 the mean annual numbers of AE-COPD-related admissions were 65 983 using the narrow definition and 107 511 using the broad definition, accounting for 1.6%—2.6% of all admissions for medical (as opposed to surgical) diagnoses among adults. The mean age of admitted patients was 73 years, regardless of the definition used; 68% of the patients were men, and the median LOS was 9 days (Table 2). An associated diagnosis of asthma was noted in 6% of records and was more frequent among women (10%) than men (4%). The in-hospital lethality was 6% for the narrow definition and 8% for the broad definition, and was higher among men (6% and 9%, respectively) than among women (5% and 7%, respectively).

Between 1998 and 2007 the annual number of hospital admissions related to AE-COPD increased by 38% (narrow definition) and 31% (broad definition). Using the narrow definition, mean age increased from 72 to 73 years, while the proportion of men decreased from 72% to 68%, the in-hospital lethality decreased from 7.6% to 6.0%, and the

Table 2 Characteristics of hospital admissions related to acute exacerbation of COPD (narrow definition) in patients aged 25 years or more; France, 1998—2007.

	Period				
	1998—9	2000—1	2002—3	2004—5	2006—7
Mean annual number	47 977	49 112	53 925	61 663	65 983
Mean age (y), (sd)	72.0 (11.8)	72.0 (11.9)	72.4 (12.0)	72.9 (11.9)	73.3 (12.1)
Age groups, years (%)					
25-44	2.3	2.3	2.2	1.9	1.9
45—64	20.5	20.4	20.2	20.0	20.4
65—84	62.4	62.5	63.8	64.3	61.7
85 or more	14.8	14.8	13.8	13.8	16.0
Men (%)	72	72	71	70	68
Median LOS[a] (days), [IQR] [b]	10 [6—16]	10 [6—15]	10 [6—15]	9 [6—15]	9 [6—14]
Records with an associated diagnosis of asthma (%)	7.6	6.9	6.6	6.5	6.1
In-hospital mortality (%)	7.6	7.1	7.5	6.7	6.0

[a] LOS: length of hospital stay.
[b] IQR: interquartile range.

proportion of records mentioning asthma decreased from 7.6 to 6.1% (Table 2). Similar trends were found when the broad definition was used (data not shown).

The frequency of ICD-10 codes specific for AE-COPD (J44.0 and J44.1) increased between 1998 and 2007 (Fig. 1).

Hospitalization rates

From 1998 to the end of 2007, the crude annual admission rates for AE-COPD increased among both men and women (+29% and +60%, respectively, for the narrow definition and +22% and +46%, respectively, for the broad definition). In 2007 these rates were 23/10 000 among men and 10/10 000 among women when the narrow definition was used, and respectively 38/10 000 and 16/10 000 with the broad definition.

The age-specific rates of AE-COPD-related admissions increased with age, particularly among adults aged 45 years or more, up to 90 years (Fig. 2).

Whatever the definition used, the age-standardized hospital admission rates for AE-COPD increased between 1998 and 2007 (Fig. 3). The interaction term between gender and year of admission was statistically significant ($p < 0.001$), with a more pronounced increase in women. The annual percentage change (APC) was +4.4 per year [95% CI: 4.2−4.6] among women and +1.6% [1.5−1.7] among men when the narrow definition was used, and respectively +3.8 [3.6−3.9] and +1.2% [1.1−1.3] when the broad definition was used.

Seasonal pattern

Admissions for AE-COPD showed a strong seasonal pattern (Fig. 4), being most frequent between December and April. The height of the peaks varied year on year, the highest peaks being observed in years with the highest rate of general practitioner visits for influenza-like illness.

Discussion

This study shows that hospitalization rates for AE-COPD in France increased between 1998 and 2007, especially among women. The seasonal pattern of hospitalization matched the incidence of GP visits for influenza-like illness.

Validity of the use of a hospital discharge database and ICD10 codes for identifying COPD exacerbations

The French hospital discharge database was created in the late 1990s, based on the diagnosis-related group (DRG) system developed in the USA. The main objective was to provide information on the activities of public and private hospitals, for financial purposes (hospital funding), but the database is also widely used for epidemiological monitoring.[15,16]

AE-COPD is particularly difficult to identify in healthcare databases. Although ICD-10 provides a specific code (J44.0 or J44.1), AE-COPD can be also designated by various combinations of diagnostic codes. In the French hospital database, the primary diagnosis was defined as the diagnosis necessitating most medical resources. Co-morbidities are frequent in COPD patients, and the primary diagnosis recorded in the database may sometimes be a complication occurring during the hospital stay rather than COPD. In addition, coding practices may be influenced by changes in diagnosis-related groups and their financial implications. Lastly, day hospitalization and stays for scheduled examinations are not identifiable in the French hospital database.

We therefore used two different indicators − a strict definition and a broader definition − and excluded short stays (less than 48 h) unless the patient died. Although the number of hospitalizations differed somewhat according to the definition used, the temporal trends and characteristics of hospitalization were very similar. The consistency with seasonal trends in GP visits for influenza-like illness also supports the validity of the algorithm used here to identify AE-COPD, as viral infections play an important role in AE-COPD. The trends observed using the narrow definition are therefore unlikely to be due to changes in coding practices.

Characteristics of hospitalization

The characteristics of hospitalization were consistent with those found in two French clinical studies.[17,18] In a cohort of

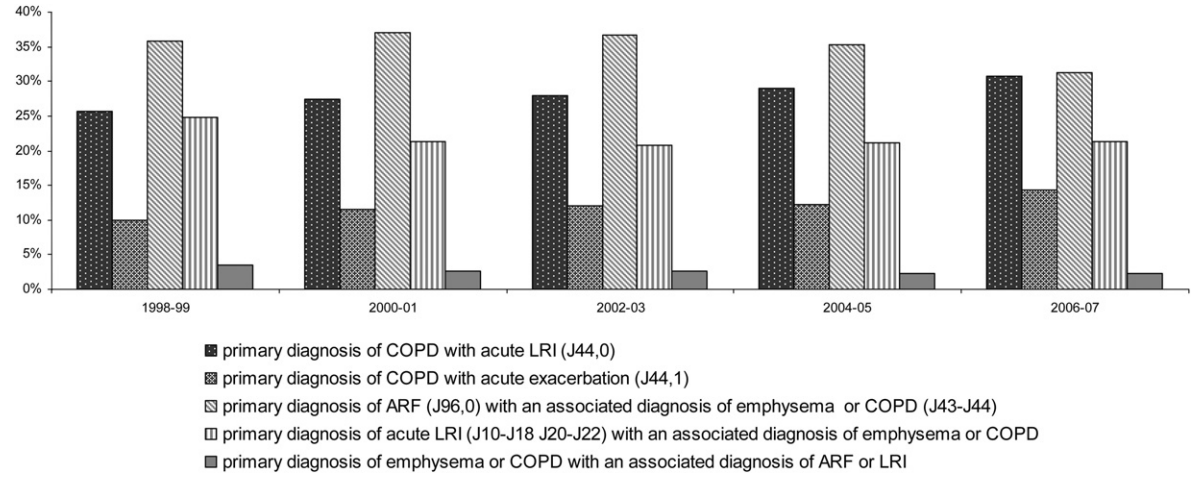

Figure 1 Distribution of the different combinations of ICD-10 codes (narrow definition) among patients aged 25 years or more hospitalized for AE-COPD; France, 1998−2007.

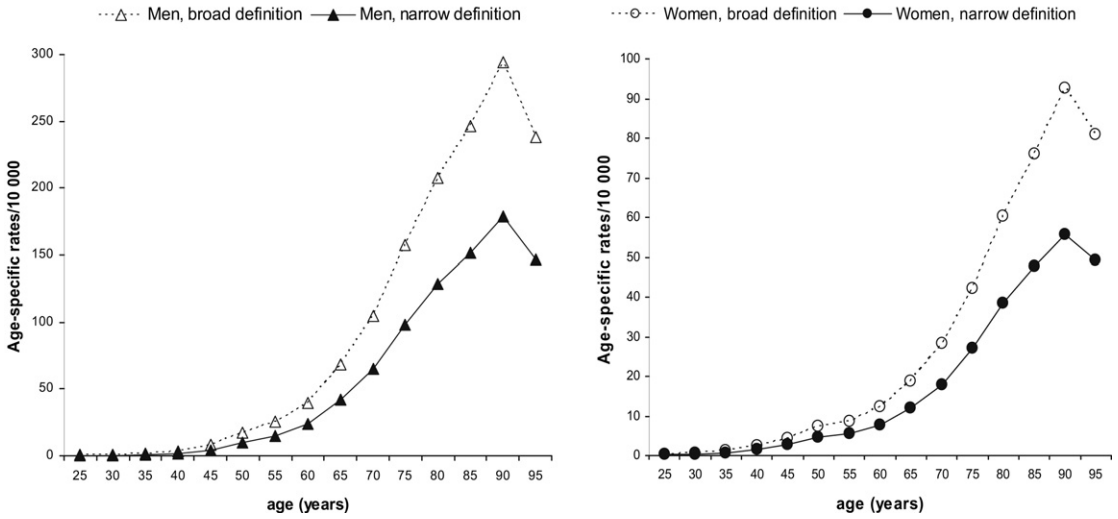

Figure 2 Mean annual age-specific rates of hospital admission related to acute exacerbations of COPD in patients aged 25 years or more; France, 2006—2007.

1824 patients admitted to medical wards for exacerbations of COPD in 2006—2007, the sex ratio (76% men), mean age (70 years) and mean length of stay (10 days) were similar to those found here.[17] In this latter study, the in-hospital lethality was low (2.5%), probably because severely ill patients who were admitted directly to an intensive care unit and died before admission to a medical ward were not included in the analysis. The in-hospital lethality in our study was 6—7%, a value close to the 8% reported by Roche et al,[18] who recruited patients in emergency rooms, providing less biased information on prognosis. Studies based on hospital discharge databases in other countries have shown in-hospital lethality of about 6—8%.[19—21]

Hospitalization rates and temporal trends

Acute lower respiratory tract infections and AE-COPD represent a major burden on the healthcare system during the winter season. We found that the annual pattern of AE-COPD admissions showed marked seasonal variations very similar to those of GP visits for influenza-like illness. This seasonal pattern of AE-COPD has already been described.[22,23] Viral infections have been found in more than 40% of patients with AE-COPD,[24,25] and viral respiratory tract infection is an important trigger of severe AE-COPD.[25,26] Recent data show that influenza vaccination is associated with fewer exacerbations and deaths among COPD patients.[27] However, although the cost of influenza vaccination is fully covered by the French national health insurance system for people over 65 years and for patients with severe chronic respiratory disease, it has been reported that only half of all patients hospitalized for an acute exacerbation of COPD had been vaccinated in the previous year.[17]

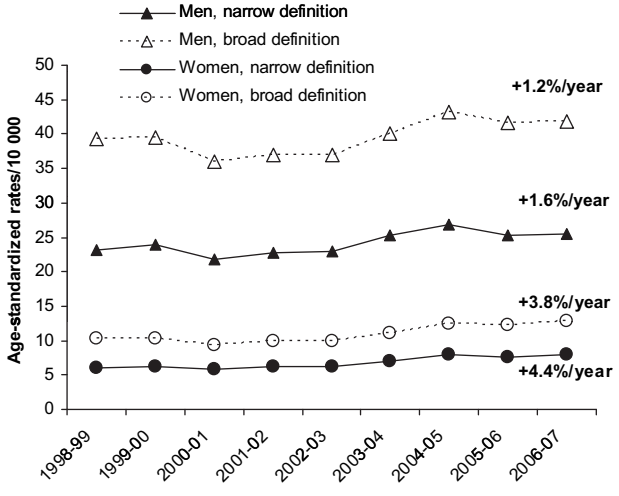

Figure 3 Age-standardized rates of hospital admission related to AE-COPD among patients aged 25 years or more; France, June 1998—July 2007. Rates are standardized to the 2006 French population and calculated from 1july to 30 june of the following year.

We were unable to study the possible correlation between AE-COPD admissions and GP visits for influenza-like illnesses because the date of admission was not available in the hospital database. Nevertheless, it is important to consider flu epidemic curves in order to avoid misinterpreting AE-COPD admission trends. We therefore divided the study period into 12-month periods, from 1 July to 30 June, in order to take into account the entire influenza epidemic period when analyzing temporal trends in AE-COPD admissions.

Admissions rates for AE-COPD increased significantly during the study period, especially among women, while overall admissions rates for medical condition slightly decreased during the same period (data not shown). Similar trends in AE-COPD admissions have been observed in other countries. The US National Hospital Discharge Survey (NHDS) collects data annually from 500 hospitals. Hospitalization rates for COPD (defined as a primary discharge diagnosis of COPD or a primary diagnosis of acute bronchitis accompanied by another listed diagnosis of COPD) increased between 1990 and 2000, and the gap between men and women disappeared.[28] Similar trends have been noted in Italy, Australia and Canada.[29—31] Between-gender differences in these trends are consistent with global trends in tobacco use and COPD epidemiology. In France, tobacco sales increased until the first tobacco law in 1976. For the last 50 years, the proportion of smokers has been increasing among women while decreasing among men.[32] As in other countries, COPD-

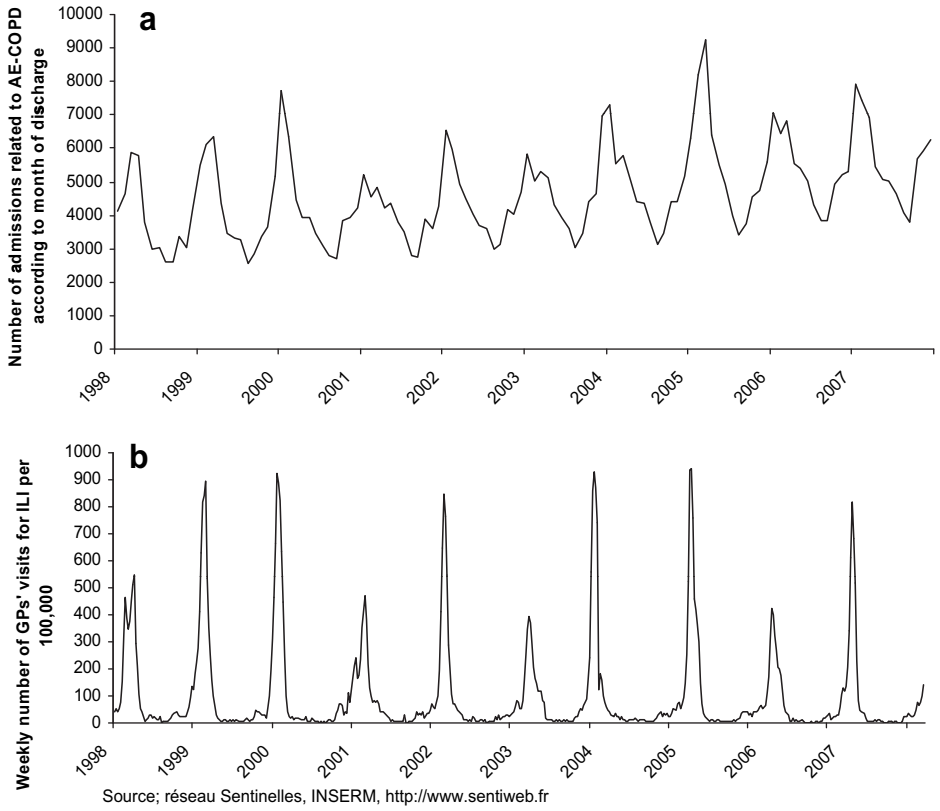

Figure 4 a) Number of hospital admissions related to acute exacerbations of COPD (narrow definition) among patients aged 25 years or more; and b) weekly incidence of general practitioner visits for influenza-like illness (ILI); France, 1998—2007.

related mortality has been increasing for the last 20 years in women, while it recently stabilized in men.[33,34] AE-COPD admissions rates and COPD-related mortality rates are still 3—4 times higher in men in France.

Several factors may explain the observed increase in hospital admissions for AE-COPD in France. One is a time-related coding bias due to better COPD awareness. Diagnostic confusion between asthma and COPD has probably become less frequent, as suggested by the decreasing proportion of admissions for COPD with an associated diagnosis of asthma. During the same period, the rates of admissions for asthma decreased among adults[35] but did not match the increase in AE-COPD admissions rates. Thus misclassification between asthma and COPD cannot fully explain the increase in COPD admissions. Another potential factor underlying the increase in admission numbers and rates is an increase in readmissions. Indeed, in-hospital lethality fell slightly during the study period (from 7.6% in 1998 to 6.0% in 2007), while mean age increased slightly, suggesting better vital outcome of severe AE-COPD. Improved patient management, and particularly the use of non-invasive ventilation, probably explains these trends.[6,36,37]

Global admission rates, by opposition to patient-based admission rates, are important to assess the global burden of a disease on the healthcare system and costs but are not sufficient to weigh improvements in care. Better diagnosis and more effective care, including the development of home-based care, may reduce hospital admissions for AE-COPD. On the other hand, better diagnosis (and therefore better coding) of COPD, and improved survival, would tend to increase the number of admissions. Further studies with linkage between hospital and national health insurance databases (including vital status) should help to determine the burden of readmissions and to assess treatment efficacy.

In conclusion, this study shows that hospitalization rates for AE-COPD have increased in France in recent years, especially among women. Vital outcome of patients admitted for AE-COPD has improved. Seasonal trends in hospital admissions for AE-COPD tend to match those of GP visits for influenza-like illness. Although the two ICD-10-based algorithms used to identify AE-COPD in the French national hospital discharge database seem to be sufficiently robust to follow temporal trends, caution should be taken with regard to misdiagnosis and coding bias.

Funding

None.

Competing interest

None.

References

1. Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet* 2007;**370**:741—50.

2. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J* 2006;**28**:523—32.
3. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007;**370**:765—73.
4. Sullivan SD, Ramsey SD, Lee TA. The economic burden of COPD. *Chest* 2000;**117**:5S—9S.
5. Detournay B, Pribil C, Fournier M, Housset B, Huchon G, Huas D, et al. The SCOPE study: health-care consumption related to patients with chronic obstructive pulmonary disease in France. *Value Health* 2004;**7**:168—74.
6. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global Strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007; **176**:532—55.
7. Biron E, Carre P, Chanez P, Crestani B, Cretin C, Dautzenberg B, et al. Le programme d'actions en faveur de la bronchopneumopathie chronique obstructive (BPCO): connaître, prévenir et mieux prendre en charge la BPCO. *Rev Mal Respir* 2006;**23**. 8S9—8S55.
8. Donaldson GC, Seemungal TA, Patel IS, Lloyd-Owen SJ, Wilkinson TM, Wedzicha JA. Longitudinal changes in the nature, severity and frequency of COPD exacerbations. *Eur Respir J* 2003;**22**:931—6.
9. Esteban C, Quintana JM, Moraza J, Aburto M, Egurrola M, Espana PP, et al. Impact of hospitalisations for exacerbations of COPD on health-related quality of life. *Respir Med* 2009; **103**:1201—8.
10. Fournier M, Tonnel AB, Housset B, Huchon G, Godard P, Verloet D, et al. Impact économique de la BPCO en France: étude SCOPE. *Rev Mal Respir* 2005;**22**:247—56.
11. Bourbeau J, Julien M, Maltais F, Rouleau M, Beaupre A, Begin R, et al. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med* 2003;**163**:585—91.
12. Casas A, Troosters T, Garcia-Aymerich J, Roca J, Hernandez C, Alonso A, et al. Integrated care prevents hospitalisations for exacerbations in COPD patients. *Eur Respir J* 2006;**28**:123—30.
13. Fuhrman C, Delmas MC. *Hospitalisations pour exacerbations de BPCO: comment les identifier à partir des données du programme de médicalisation des systèmes d'information?*. Saint-Maurice (France): Institut de veille sanitaire; 2009.
14. Réseau Sentinelles, INSERM, UPCM. Available from: http://www.sentiweb.fr [accessed 2010 May].
15. Fosse S, Hartemann-Heurtier A, Jacqueminet S, Ha VG, Grimaldi A, Fagot-Campagna A. Incidence and characteristics of lower limb amputations in people with diabetes. *Diabet Med* 2009;**26**:391—6.
16. Pascal L, Fuhrman C, Durif L, Nicolau J, Charpin D, Dujols P, et al. Evolution des hospitalisations pour asthme en France métropolitaine, 1998—2002. *Rev Mal Respir* 2007;**24**:581—90.
17. Piquet J, Chavaillon JM, David P, Martin F, Braun D, Ferrer LP, et al. Caractéristiques et prise en charge des exacerbations aiguës de BPCO hospitalisées. Etude EABPCO-CHPG du Collège des pneumologues des hôpitaux généraux. *Rev Mal Respir* 2010;**27**:19—29.
18. Roche N, Zureik M, Soussan D, Neukirch F, Perrotin DThe Urgence BPCO (COPD Emergency) Scientific Committee and investigators. Predictors of outcomes in COPD exacerbation cases presenting to the emergency department. *Eur Respir J* 2008;**32**:953—61.
19. Bustamante-Fermosel A, De Miguel-Yanes JM, Duffort-Falco M, Munoz J. Mortality-related factors after hospitalization for acute exacerbation of chronic obstructive pulmonary disease: the burden of clinical features. *Am J Emerg Med* 2007;**25**: 515—22.
20. Chen Y, Stewart P, Dales R, Johansen H, Bryan S, Taylor G. Changing age-pattern of hospitalisation risk of chronic obstructive pulmonary disease in men and women in Canada. *Age Ageing* 2005;**34**:373—7.
21. Holguin F, Folch E, Redd SC, Mannino DM. Comorbidity and mortality in COPD-related hospitalizations in the United States, 1979 to 2001. *Chest* 2005;**128**:2005—11.
22. Hansell A, Hollowell J, McNiece R, Nichols T, Strachan D. Validity and interpretation of mortality, health service and survey data on COPD and asthma in England. *Eur Respir J* 2003;**21**: 279—86.
23. Johnston NW. The similarities and differences of epidemic cycles of chronic obstructive pulmonary disease and asthma exacerbations. *Proc Am Thorac Soc* 2007;**4**:591—6.
24. Papi A, Bellettato CM, Braccioni F, Romagnoli M, Casolari P, Caramori G, et al. Infections and airway inflammation in chronic obstructive pulmonary disease severe exacerbations. *Am J Respir Crit Care Med* 2006;**173**:1114—21.
25. Seemungal T, Harper-Owen R, Bhowmik A, Moric I, Sanderson G, Message S, et al. Respiratory viruses, symptoms, and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;**164**:1618—23.
26. Hutchinson AF, Ghimire AK, Thompson MA, Black JF, Brand CA, Lowe AJ, et al. A community-based, time-matched, case-control study of respiratory viruses and exacerbations of COPD. *Respir Med* 2007;**101**:2472—81.
27. Schembri S, Morant S, Winter JH, MacDonald TM. Influenza but not pneumococcal vaccination protects against all-cause mortality in patients with COPD. *Thorax* 2009;**64**:567—72.
28. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance—United States, 1971—2000. *MMWR Surveill Summ* 2002;**51**:1—16.
29. Agence de la santé publique du Canada. *la vie et le souffle: les maladies respiratoires au Canada, 2007*. Ottawa: Agence de la santé publique du Canada; 2007.
30. Trerotoli P, Bartolomeo N, Moretti AM, Serio G. Hospitalisation for COPD in Puglia: the role of hospital discharge database to estimate prevalence and incidence. *Monaldi Arch Chest Dis* 2008;**69**:94—106.
31. Wilson DH, Tucker G, Frith P, Appleton S, Ruffin RE, Adams RJ. Trends in hospital admissions and mortality from asthma and chronic obstructive pulmonary disease in Australia, 1993—2003. *Med J Aust* 2007;**186**:408—11.
32. Hill C, Laplanche A. *Le tabac en France: les vrai chiffres*. Paris: La documentation Française; 2003. 140 pp.
33. Chapman KR, Mannino DM, Soriano JB, Vermeire PA, Buist AS, Thun MJ, et al. Epidemiology and costs of chronic obstructive pulmonary disease. *Eur Respir J* 2006;**27**:188—207.
34. Fuhrman C, Jougla E, Nicolau J, Eilstein D, Delmas MC. Chronic obstructive pulmonary disease deaths in France, 1979—2002: a multiple-cause analysis. *Thorax* 2006;**61**:930—4.
35. Delmas MC, Fuhrman C. L'asthme en France: synthèse des données épidémiologiques descriptives. *Rev Mal Respir* 2010; **27**:151—9.
36. Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995; **333**:817—22.
37. Lightowler JV, Wedzicha JA, Elliott MW, Ram FSF. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. *BMJ* 2003;**326**:185.